REMARKS

Claims 1-14 remain pending for prosecution in the present application.

The Rejections under 35 U.S.C. § 102

Claims 1, 2 and 10-14 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Claffey et al. Additionally, Claims 1-3, 10-12 and 14 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Pötgens et al. Applicants respectfully traverse the rejections.

The presently claimed invention is directed to antagonists of VEGF activity. As is recited in the claims, these VEGF antagonists are VEGF polypeptides having one or more mutated cysteine residues which inhibit the molecules from properly dimerizing. However, as is explicitly recited in the claims, these molecules retain the ability to bind to the VEGF receptor. It is this property that makes them effective as antagonist molecules, i.e., their ability to bind to and occupy a VEGF receptor, thereby preventing wild-type VEGF from binding to that receptor and activating VEGF activity.

Claffey et al. teach a variety of murine VEGF mutants that are incapable of inducing VEGF activity. Specifically, in Figure 7, Claffey et al. demonstrate that a variety of cysteine residue mutants of VEGF have no biological activity. However, what is notable about the Claffey et al. disclosure is that it does not teach, suggest nor even contemplate that these mutant VEGF molecules would retain the ability to bind to the VEGF receptor and, thereby effectively function as a VEGF antagonist as presently claimed. In this regard, the Examiner must keep in mind that for a mutant VEGF polypeptide to function as an antagonist

molecule as presently claimed, it must be able to bind to and occupy the VEGF receptor. The Claffey et al. article does not teach this.

Like Claffey et al., Pötgens et al. also teach disruption of cysteine residues in the VEGF polypeptide to obtain monomeric VEGF, however, do not teach nor suggest that such variant polypeptides would retain the ability to bind to and occupy VEGF receptors.

The Examiner, however, asserts that notwithstanding the fact that Claffey et al. and Pötgens et al. do not demonstrate that their mutant VEGF polypeptides bind to the VEGF receptor, such properties are "inherently" possessed, thereby still anticipating the claimed invention. Applicants respectfully disagree.

In this regard, Applicants wish to respectfully point out that the standards for inherency under 35 U.S.C. § 102 are clear. The fact that a prior art article may inherently have the characteristics of the claimed invention is not sufficient to support a rejection under 35 U.S.C. § 102; rather, the inherency must be certain. See Ex parte Skinner, 2 USPQ2d 1788 (BPAI 1986) and Ex parte Cyba, 155 USPQ 756 (POBA 1966). Moreover, "inherency must be a necessary result and not merely a possible result". In re Oelrich, 212 USPQ 323 (CCPA 1981) (emphasis supplied).

Furthermore, there is a great deal of case law and other material supporting the idea that an "accidental" duplication of a claimed invention that was not intended nor appreciated cannot constitute anticipation under 35 U.S.C. § 102. In this regard, the Examiner is respectfully directed to Exhibit A attached herewith which is an excerpt from "*Lipscomb's Walker on Patents*",

3rd ed., Bancroft-Whitney, San Francisco (1984) which clearly discusses the doctrine of "accidental" anticipation and how such does not constitute anticipation under 35 U.S.C. § 102.

Also, in In re Marshall, 198 USPQ 344 (CCPA 1978), the CCPA stated: "[a]n accidental or unwitting duplication of an invention cannot constitute an anticipation." (Emphasis supplied). In Marshall, the rejected claims were drawn to a method of controlling weight gain by orally administering a drug containing the anesthetic, oxethazaine. The claims were rejected over prior art references which also taught the oral administration of oxethazaine, but for a different use, i.e., for the purpose of treating peptic ulcers and other gastrointestinal disorders. Nothing in the prior art references taught, suggested or even contemplated that the oral administration of oxethazaine would be effective for controlling weight gain.

The CCPA reversed the rejection of the claims reasoning that although the prior art taught the oral administration of oxethazaine (i.e., the same method step as recited in the disputed claims) and taught that it was effective for treating gastrointestinal disorders, it was completely silent as to its property for effectively controlling weight gain. Therefore, the CCPA concluded that claims directed to a method for controlling weight gain comprising the oral administration of oxethazaine could not be unpatentable over the cited prior art.

By analogy with Marshall, although the herein cited art may teach the disruption of cysteine residues in the VEGF protein to obtain monomeric VEGF polypeptides, the cited art is completely silent as the ability to obtain variant VEGF polypeptides that retain the ability to bind to VEGF receptors and thereby

function as VEGF antagonists. As such, by analogy with Marshall, Applicants respectfully submit that the present claims are patentable over the herein cited Claffey et al. and Pötgens et al. articles.

Finally, the Examiner is directed to In re Newell, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989) wherein the Federal Circuit stated:

> "a retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements of the particular claimed combination."

In light of the above, while Claffey et al. and Pötgens et al. may teach the disruption of cysteine residues in the VEGF polypeptide, they do not teach nor suggest that such variant VEGF polypeptides may retain the ability to bind to and occupy the VEGF receptor. Claffey et al. and Pötgens et al. merely report that such variant polypeptides are "inactive". Thus, Applicants respectfully submit that Claffey et al. and Pötgens et al. do not inherently anticipate the presently claimed invention under the applicable case law as described above. Applicants, therefore, respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102.

The Rejections under 35 U.S.C. § 103

Claim 13 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Pötgens et al. Claims 4-6 and 9 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Pötgens et al. Finally, Claims 7 and 8 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Pötgens et al. in view of Pang. Applicants respectfully traverse the rejections.

In traversal, Applicants again note that Pötgens et al. do not teach nor suggest that their cysteine residue mutants are capable of binding to VEGF receptors and, therefore, do not teach that their mutant VEGF polypeptides are capable of functioning as effective VEGF antagonists.

Moreover, nothing in the Pötgens et al. article teaches or suggests to one of ordinary skill in the art how to go about obtaining VEGF antagonist molecules that retain the ability to bind to VEGF receptor, thereby functioning as antagonists of VEGF activity. Only in the present application was it demonstrated that VEGF antagonists which retain the ability to bind to and occupy VEGF receptors could be obtained.

Additionally, the cited Pang reference does nothing to remedy the above described defect of the Pötgens et al. article. Pang teaches or suggests nothing about the ability to obtain VEGF antagonist polypeptides which retain the ability to bind to and occupy VEGF receptors on cells.

The Examiner, however, again asserts that the presently claimed invention is rendered "inherently" obvious by the cited art. Applicants respectfully disagree.

In this regard, the Examiner is respectfully directed to In re Spoorman, 150 USPQ 449, 452 (CCPA 1966), wherein the Court of Customs and Patent Appeals stated:

> "The inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." (Emphasis supplied). (See also, In re Adams, 148 USPQ 742 (CCPA 1966), In re Naylor, 152 USPQ 106 (CCPA 1967) and In re Chapman, 148 USPQ 711 (CCPA 1966)).

Furthermore, in Kloster Speedsteel AB v. Crucible, Inc., 230 USPQ 81, 88 (Fed. Cir. 1986), the Federal Circuit stated that "[i]nherency and obviousness are distinct concepts". As such, an inherent feature of an invention may be relied upon to establish obviousness only if that inherent feature itself would have been obvious to one of ordinary skill in the art.

Thus, under established case law, even assuming *arguendo* that the mutant polypeptides disclosed by Pötgens et al. were to "inherently" possess the ability to bind to VEGF receptors, the fact that that property was "unknown" to Pötgens et al. and simply could not have been gleaned by a skilled artisan from a reading of the Pötgens et al. article absolutely precludes a finding that Pötgens et al. renders the presently claimed method obvious under 35 U.S.C. § 103.

In light of the above, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. § 103.

On the basis of the amendments and remarks presented herein, we believe that this application is now in condition for immediate allowance and

respectfully request the Examiner to withdraw the outstanding rejections and pass this application to issue.

Respectfully submitted,

FLEHR HOHBACH TEST
ALBRITTON & HERBERT LLP

Mark T. Kurnal REG NO: 42,767

FOR: Walter H. Dreger
Reg. No. 24,190

Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989